suppressed the secretion of TNF-α and IL-1β by peritoneal macrophages. The most potent silencing effects was 90% and 60% suppression, respectively. Fluorescent labeled siRNA was found to be transduced into almost all of the cells. TNF-α and IL-1β mRNA level of siRNA transfected synovial fibroblasts were 0.3 fold and 0.2 fold of control cells.
Conclusions: RNA interference (RNAi) is the powerful means of silencing genes, and the effect is sequence specifically. Recently, several studies applied RNAi to treat of various disorders in animal models, and showed that RNAi may improve promissing strategies to treat human diseases by silencing disease-responsible genes *in vivo*. In the pathogenesis of osteoarthritis (OA) and rheumatoid arthritis (RA), various inflammatory cytokines produced by synovium leads to destruction of joints. In particularly, TNF-α and IL-1β is known as a key mediator of OA and RA. Therefore, to suppress the expression of TNF-α and IL-β in joints *in vivo* is expected an effective and less invasive conservative therapy of joint disease. In this study, TNF-α or IL-1β specific siRNA were transduced into synovial fibroblasts successfully, and suppress the expression of TNF-α and IL-1β in synovial fibroblasts *in vitro*.

P224

ASSOCIATION OF THE MATRIX METALLOPROTEINASE 1 POLYMORPHISM WITH PROGRESSION OF KNEE OSTEOARTHRITIS

A Osawa[1], T Kimura[2], M Nozawa[1], S Moriya[3], N Seki[4], M Muramatsu[2], H Kurosawa[1]
[1]Department of Orthopaedic Surjery, Juntendo University School of Medicine, Tokyo, Japan; [2]Molecular Epidemiology, Medical Research Institute, Tokyo Medical and Dental University, Tokyo, Japan; [3]Department of Biochemistry and Genetics, Chiba University Graduate School of Medicine, Chiba, Japan; [4]Department of Functional Genomics, Chiba University Graduate School of Medicine, Chiba, Japan

Objective: Matrix metalloprotenases (MMPs) are the most critical proteinases to degrade the extracellular matrix of OA cartilage. The objective of this study is to investigate the association between MMP-1 single nucleotide polymorphisms (SNPs) and primary knee OA progression.
Subjects: The medical records and DNA samples were obtained from 418 unrelated Japanese, 115 non-OA subjects and 303 knee symptomatic primary knee OA patients having radiographic grade 3 or more (mean age of 76.2 ± 8.0, 65 males and 353 females). Non-OA population consisted of volunteers without any symptom and/or sign of OA who had visited these hospitals for fractures, injured or other orthopedic disease. Genotyping was performed using LightTyper and melting curve analysis.
Results: Three SNPs were not in linkage disequilibrium. As we found one genotype frequency was significantly different between the OA progression stages, we hereafter focused on this SNP, 1655A/G. The frequencies of *AA* and *AG+GG* group subjects in stage 1-2, 3 and 4 were 0.28, 0.40, 0.32 and 0.25, 0.53, 0.22, respectively ($P = 0.0190$). Age BMI, and sex ratio were not different significantly between these genotype groups. Therefore, we hypnotized that *AA* group subjects more likely to progress OA. Indeed, the medial tibiofemoral joint spaces were narrower in *AA* group subjects (adjusted to age, sex and BMI, $P = 0.0158$). Moreover, this tendency was apparent in the highest tertile of BMI (> 25.8, $P = 0.0160$) whereas those in the lowest and middle groups were not different significantly.
Conclusion: This study suggested that one SNP in MMP1 is associated with knee OA severity. This SNP could be a useful marker to prospect the progression of knee OA. It might be better to recommend the patients who possess the risk genotype to reduce body weight for slowing the progression. Further investigation of the molecular aspects of this SNP, or the searching other truly responsible SNPs may clarify the role(s) of MMP1 in the cartilage and the mechanisms of OA progression.

P225

DOES TROCHLEAR CARTILAGE ANALYSIS FROM QUANTITATIVE MAGNETIC RESONANCE IMAGING PROVIDE INFORMATION THAT PATELLAR ANALYSIS DOES NOT?

ME Schutzer[1], F Eckstein[1], DJ Hunter[2], M Hudelmaier[1], C McClennan[2], JB Niu[2], DT Felson[2]
[1]Institute of Anatomy & Musculoskeletal Research, Paracelsus Medical Private University, Salzburg, Austria; [2]Clinical Epidemiology Research and Training Unit, Boston University School of Medicine, Boston, MA

Aim: Patellar and femoral (trochlear) cartilage morphology cannot be evaluated separately on plain radiographs. Quantitative MR imaging, however, can provide these data with high accuracy and precision, but it is unclear whether it is sufficient to measure just the patella, or whether measurement of trochlear cartilage provides additional information. We therefore analyzed the correlation of patellar and trochlear cartilage morphology with quantitative MR imaging in knees with and without radiographic evidence of patellofemoral OA (PFOA) in a community sample.
Methods:186 subjects from the Framingham cohort (138 women, 48 men, age 61 ± 7.8 y) were studied. Patellar cartilage morphology was determined from axial MR images (FLASH VIBE we sequence, $1.5 \times 0.31 \times 0.31$ mm^3 resolution), and trochlear cartilage morphology from sagittal images, acquired with the same sequence. We determined total area of subchondral bone (tAB), percent denuded area of subchondral bone (dAB%), mean and maximal cartilage thickness, and cartilage volume (VC), by using proprietary software (Chondrometrics GmbH, Ainring, Germany). PFOA status was evaluated on lateral radiographs, with PFOA being defined as presence of osteophytes grade ≥ 2, or presence of osteophytes grade ≥ 1 with JSN grade ≥ 2 in the PF joint.
Results: Of 176 cases without radiographic PFOA, 18.8% displayed areas of denuded cartilage in the patella (dAB% = 0-36%), 12.5% in the trochlea (0-18%), and 5.7% in both surfaces. Of 10 cases with PFOA, 60% displayed areas of denuded cartilage in the patella (0 to 57%), 80% in the trochlea (0 to 23%), and 50% in both surfaces. Patellar cartilage thickness differed significantly ($p < 0.01$) in women with (n = 9) and without PFOA (n = 129), but interestingly trochlear cartilage did not. The correlations between patellar and trochlear cartilage in subjects with/without PFOA were r = 0.47/0.61 for tAB, r = 0.87/0.62 for VC, and r = 0.58/0.42 for mean cartilage thickness.
Conclusions: Denuded cartilage can be seen in a substantial proportion of subjects with apparently normal lateral radiographs. There are a number of subjects with denuded trochlear cartilage, who do not display denuded patellar cartilage at the same time (6.8% in subjects without PFOA, and 30% in subjects with PFOA). Also, there only exists a moderate correlation between patellar and trochlear cartilage morphology in subjects with and without radiographic PFOA, with 22% to 76% of the variability in cartilage morphology of the trochlea being explained by the variability in the patella. In summary, lateral radiographs fail to detect areas of full thickness cartilage loss in a considerable number of subjects. The results also indicate that analysis of trochlear cartilage morphology may provide unique and important information in addition to measurement of cartilage morphology in the patella.